Office Action Summary	Application No.	Applicant(s)	
	10/608,915	HOFFMAN ET AL.	
	Examiner	Art Unit	
	Pablo Whaley	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *85-92 and 107-118* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *85-92 and 107-118* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request For Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/05/2007 has been entered.

Claims Under Examination

Claims 85-92 and 107-118 are herein under examination. Claims 1-84 and 93-106 have been cancelled.

Priority

Priority to US Provisional Application 60/392,843, filed June 28, 2002, has been acknowledged.

Withdrawn Rejections

The rejection of claims 85-92 and 114-115 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's amendments filed 10/5/2007.

The rejection of claims 85, 87-90, 92, and 109-115 under 35 U.S.C. 103(a) as being made obvious by Yaffe et al. (Nature Biotechnology, April 2001, Vol. 19, p.348-353), in view of Geetha et al. (Protein

Engineering, 1999, Vol. 12, No. 7, p.527-534) is withdrawn in view of applicant's arguments filed 10/5/2007.

The rejection of claims 85-92 and 109-118 under 35 U.S.C. 103(a) as being obvious by Rognan et al. (J. Med. Chem., 1999, Vol. 42, p.4650-4658), in view of Yaffe et al. (Nature Biotechnology, April 2001, Vol. 19, p.348-353) is withdrawn in view of applicant's arguments filed 10/5/2007.

Claim Rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 85-92, 107-109, 111, and 118 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims that depend directly or indirectly from claims 85 and 90 are also reject due to said dependence.

Claims 85, 90, 107, 111, and 118 recite “outputting a result from the above steps." It is unclear which “result” of the above steps applicant is referring to as being output.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 85-92, 107-109, 111, and 118 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. These claims are rejected for the following reasons.

The instant claims are drawn to methods of assessing the binding affinity between a candidate peptide and target sequence. For a process to be statutory, it must provide: (1) a practical application by physical transformation (i.e. reduction of an article to a different state or thing), or (2) a practical application that produces a concrete, tangible, and useful result [State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998)], [AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)]. As noted in State Street Bank & Trust Co. v. Signature Financial Group Inc. CAFC 47 USPQ2d 1596 (1998), the statutory category of the claimed subject matter is not relevant to a determination of whether the claimed subject matter produces a useful, concrete, and tangible result. The question of whether a claim encompasses statutory subject matter should not focus on which of the four categories of subject matter a claim is directed to a process, machine, manufacture, or composition of matter--but rather on the essential characteristics of the subject matter, in particular, its practical utility.

In the instant case, the claimed processes do not result in a physical transformation of matter. Where a claimed method does not result in a physical transformation of matter, it may be statutory where it recites a result that is concrete (i.e. reproducible), tangible (i.e. communicated to a user), and useful result (i.e. a specific and substantial). Claims 85, 90, 107, 111, and 118 all result in "outputting a result

from the above steps." This is not a tangible result because outputting a "result of the above steps" does not communicate a specific result in a user readable format. Therefore the claimed method does not recite a practical application of a 35 U.S.C. 101 Judicial exception and is not statutory.

This rejection could be overcome by amendment of the claims to recite that a result of the process is outputted to a display, or to a user, or in a graphical format, or in a user readable format, or by including a result that is a physical transformation. The applicants are cautioned against introduction of new matter in an amendment. For an updated discussion of statutory considerations with regard to non-functional descriptive material and computer-related inventions, see the Guidelines for Patent Eligible Subject Matter in the MPEP 2106, Section IV.

Response to Arguments

Applicant's arguments, filed 10/05/2007, that the claims are statutory view of the claim amendments have been fully considered but are not persuasive. The instant claims now recite "outputting a result from the above steps." The claims do not result in a physical transformation of matter. Where a claimed method does not result in a physical transformation of matter, it may be statutory where it recites a result that is concrete (i.e. reproducible), tangible (i.e. communicated to a user), and useful result (i.e. a specific and substantial). However, as set forth above, claims 85, 90, 107, 111, and 118 all result in "outputting a result from the above steps." While outputting a result is generally considered to be a "tangible" result, it is unclear what specific result is actually being output to the user (see 112 2nd rejection above). Therefore the claims do not communicate a specific result in a user readable format. Therefore the claimed method does not recite a practical application of a 35 U.S.C. 101 Judicial exception and is not statutory.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 85-92 and 109-118 are rejected under 35 U.S.C. 103(a) as being obvious by Rognan et al. (J. Med. Chem., 1999, Vol. 42, p.4650-4658), in view of Welch et al. (Chemistry & Biology, 1996, Vol. 3 No. 6, p.449-462).

Rognan et al. teach structure-based method for predicting the binding free energy of candidate peptides to MHC class I proteins [Abstract], as set forth in the previous office action mailed 08/09/2006. More specifically, Rognan et al. teach the following aspects of the instantly claimed invention: a database of MHC proteins and MHC-bound candidate peptides [Fig. 1]; predicting binding scores (i.e. affinities) using a predictive method that incorporates linear equations [Fig. 1 and 2]; linear regression analysis (i.e. linear scaling) of the affinity data from each scoring model before they are combined [p.4657, Statistical Analyses]; normalization (i.e. scaling) of data values between 0 and 1 [Fig. 4], and combining affinity data to determine a single predictive binding affinity [Fig. 1], as in instant claims 85, 87, 89, 90, 92, 109-

112. The above method taught by Rognan et al. is reasonably interpreted as combining a plurality of distinct predictive scoring methods to determine an overall predictive score in view of the specification, which teaches scoring by individual methods and combining "scores" to determine an overall ranking for peptide binding [Specification, Fig. 2 and 3]. Rognan et al. also teaches specific antigen binding domains for MHC proteins [p.4655, Col. 2, ¶ 1], which is a teaching for epitopes, as in claims 86 and 91, which are well-known to bind to MHC proteins. Rognan et al. also teach a predictive model applied to nonameric ligands [p.4654, Col. 2, 2], as in instant claim 88. Rognan et al. also teach mathematical functions and computing protocols for carrying out the above method [p.4566, Experimental Section] and displaying results [Fig. 3], which is an implicit teaching for outputting results and a user and a memory, as in claims 95, 90, 107-112, 114, and 115. Rognan also shows free energy binding scores and peptide binding based on IC-50 values [See Table 1 and p.4655, Experimental Section], as in claims 116-118.

Rognan et al. do not specifically teach predicting a second affinity by evaluating sequence and binding information with a second predictive method, as in instant claims 85, 90, and 107-112.

Welch et al. teach a fully automated predictive method (Hammerhead) for assessing binding affinity of protein-ligand complexes. In particular, Welch teaches a nonlinear scoring function that predicts binding affinity and allows for model refinement to improve the overall score [p.450, Results and Discussion] and adjustable scoring parameters [Table 2], and averaged (i.e. scaled) scoring values less than 1 [Table 3]. Welch also teaches a docking algorithm that maximizes the scoring function to improve affinity prediction [p.451, Col. 2].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the structure-based predictive method taught by Rognan et al. in combination with the automated predictive method taught by Welch et al., since Rognan et al. suggest combining different predictive methods for determining binding affinity [Fig. 1 and p.4644, Col. 1, ¶ 3]. One of ordinary skill in the art would have been motivated to additionally use the automated secondary predictive method of

Welch since it improves affinity prediction of different ligands at the same site [p.449, Col. 2 and p.450, Col. 1] and eliminates human bias in protein docking site selection [p.458, Col. 1]

Response to Arguments

Applicant's arguments, filed 10/5/2007, that Yaffe's binding scores are not a measure of affinity and that Yaffe does not teach determining a first and second affinity are moot in view of the new grounds of rejections.

Applicant's arguments, filed 10/5/2007, that Rognan does not teach a first and second methods for determining affinities for a candidate peptide for a target protein have been fully considered but are not persuasive. Rognan does not specifically teach predicting a second affinity by evaluating sequence and binding information with a second predictive method, as in instant claims 85, 90, and 107-112. However, Rognan shows a first method for determining binding scores (i.e. affinities) that is based on sequence data and binding affinity information and includes five different predictive methods [Fig. 1]. Predictive scores are then combined and evaluated to determine a single predictive binding affinity [Fig. 1]. Thus, in view of the teachings of Rognan and the specification [Fig. 2 and 3], Rognan at a minimum suggests the use of a plurality of predictive methods and combining individual "scores" to determine an overall ranking for peptide binding.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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